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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,452	07/13/2001	Mohammad Sarwar Nasir	01-660	5761

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EXAMINER	
DAVIS, DEBORAH A	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,452	NASIR ET AL.	
	Examiner	Art Unit	
	Deborah A. Davis	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' response to the Office Action mailed on September 10, 2004 has been acknowledged. Currently, claims 1-18 are pending and under consideration.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-4 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable Dixon et al (USP#4,835,100) in view of Nasir et al (Combinatorial Chemistry & High Throughput Screening, 1999, 2, 177-190).

Dixon et al teaches a method and a test kit for detecting an aflatoxin B1 using monoclonal antibodies (See abstract and column 3, lines 16-19). The antigens or antibodies to aflatoxins are conjugated to a label (see abstract) and more specifically, horseradish peroxidase (column 6, lines 34-37) and BSA (column 5, lines 12-14). Dixon et al explains that aflatoxin B1 is converted to aflatoxin B1-oxime for labeling (column 4, lines 62-68 and column 5, lines 1-15). Dixon et al explains that aflatoxins are toxic metabolites and they can act as potent carcinogens, mutagens and teratogens and are known to occur naturally in wheat and other foods (col. 1, lines25-34) and (col. 10, lines 45-52). Dixon et al uses methanol as an extraction solvent (col. 11, lines 36-47). ELISA assay methods were used for detection of aflatoxins (column 7, lines 1-5).

The reference of Dixon does not teach the detection of aflatoxins in a Fluorescent Polarization Assay format, however, Nasir et al teaches field tests to determine mycotoxins (a form of aflatoxins) in human, animal and grain diseases. (pg. 18, last para.). Nasir et al teaches a homogenous assay using fluorescence polarization to analyze these mycotoxins in grains (See abstract). Mycotoxins that are extracted from grains, with a suitable solvent and the sample are added into the antibody solution. A mycotoxin antigen of interest is labeled with a fluorescent molecule (tracer) and is added to the antibody solution. Once the reaction takes place, the fluorescent polarization of the tracer is then measured (pg. 182, para. 1). Nassir et al also teaches that using fluorescent polarization assays has good sensitivity and the possibility of obtaining results rapidly without any separation and purification steps make Fluorescent Polarization more attractive than methods where one needs to physically separate the bound and unbound species before analysis.

Therefore, it would have been obvious to one of ordinary skill in the art to modify the reference of Dixon et al to detect aflatoxins utilizing Fluorescent Polarizations assay as taught by Nasir et al because this type of assay is sensitive and results can be obtained rapidly without any separation and purification steps. One would be motivated because detect a variety of forms of mycotoxins which includes aflatoxins because they are known toxins found in grains and can pose health risks.

4. Claims 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dixon in view of Nasir et al, and further in view of and further in view of Michel et al (USP#5,741,654).

The teachings of Dixon et al in view of Nasir et al are set forth above and differ from the instant claims in not particularly pointing out a particular type of fluorescein used in the assay.

However, Michel et al discloses a Fluorescence Polarization assay for the quantification of antibodies in which a variety of fluoresceins are used as detectable moiety components of tracers, such as one mentioned in particular, the 6-aminofluorescein moiety (isomer II of fluorescein) which is one of the preferred moieties of choice in the said assay (col. 8, lines 1-22).

It would have been obvious to one of ordinary skill in the art to employ a fluoresceinamine or its isomers as binding moieties because such structures are well known in the art to work well in Fluorescence Polarization Immunoassays for quantitation of a sample. In addition, the fluorescein used for labeling in this assay would have been a functional equivalent of the fluorescent molecule used for labeling in the assay of Dixon et al in view of Nasir et al - wherein both would have worked equally as well absent unexpected results.

5. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dixon et al in view of Nasir et al and further in view of McMahon et al (USP#5,166,078).

The teachings of Dixon et al in view of Nasir et al are set forth above and differ from the instant claims in not teaching the construction of a standard curve using a plurality of different known concentrations of aflatoxin.

However, McMahon et al teaches a method for measuring a hapten that is poorly soluble in an aqueous solution such as aflatoxins (col. 2, lines 45-53). The invention permits fast, safe, and convenient measurements of haptens, which are either insoluble or unstable in aqueous solution by providing standards that are soluble and stable in aqueous solution. The standards are used to determine the amount of haptens that are present in the assay (col. 1, lines 43-48). To determine the amount of hapten in a sample, the reaction of the hapten and the antibody is compared to the reaction of the hapten-conjugate and the antibody. The conjugates of the invention are used as controls in standard immunoassay (col. 2, lines 29-40). The reactivity of the conjugate was compared to aflatoxin standards and a standard curve was created relating aflatoxin levels to aflatoxin-conjugate levels (col. 3, lines 9-16).

It would have been obvious to one of ordinary skill in the art to use a plurality of aflatoxins in standard solutions having different known concentrations and comparing them with aflatoxin-conjugates to create a standard curve to permit fast, safe and convenient measurements of haptens. Further, one skilled in the art would know that certain levels of aflatoxins found in different amounts of grain are toxic to human and animals and a standard curve is needed to compare those levels that would be of concern.

6. Claims 11-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nasir et al in view of Dixon et al.

The teachings of Nasir et al are set forth above and differ from the reference of Dixon in not teaching a kit.

However, Dixon et al however discloses a kit for afltoxins and explains that obvious variations of preparing a kit for convenience will be apparent to those skilled in the art and points out that kits are well developed in the patent arts and literature (col. 12, lines 28-33).

It would have been prima facie obvious to one of ordinary skill in the art to take the assay for aflatoxins as taught by Dixon et al, combined with the teachings of Nasir et and formulate a kit. Further, it would be convenient to do so because one can enhance sensitivity of a method by providing reagents as a kit. In addition, the reagents in a kit are available in premeasured amounts, which eliminates the variability that can occur when performing the assay.

Response to Arguments

7. Applicant's arguments with respect to the reference of Dhar is noted, but have been considered but are moot in view of the rearrangement of the prior art references already applied. Therefore, the reference of Dhar is hereby withdrawn.

8. Applicant argues that there is no prior art teaching of a reasonable expectation of success that the tracer (aflatoxin oxime conjugated to a fluorophore) has the special property of being able to bind to an antibody specific for aflatoxin to produce a detectable change in fluorescence polarization. Applicant further argues that the reference of Nasir et al teaches labeling mycotoxin antigens with a fluorescent molecule and there is not prior art teaching that the product would have the special property of being able to bind to an antibody to produce a detctable change in fluorescence polarization. These arguments are noted but not found to be persuasive. The reference of Dixon et al teaches that it would be "advantageous to use monoclonal antibodies for conducting the immunoassays for aflatoxin B1" and "The monoclonal antibodies can then be used in the development of a colorimetric commercial assay systems for mycotoxins (which are forms of aflatoxins) such as enzyme linked immunosorbent assay (ELISA) or fluorescent antibodies tests" (column 2, lines 21-30). The reference of Dixon et al teaches aflatoxin oxime conjugated to BSA label (column 4, lines 68 to column 5, lines 1-16) and antibodies for its detection, the reference of Nasir et al teaches mycotoxins conjugated to fluourophore and reacted with antibodies. Therefore, it is the examiner's position fluorphore labels versus BSA labels are equal equivalents because both are used for detections purposes and are reacted with their respective antibodies. See newly formed rejection above.

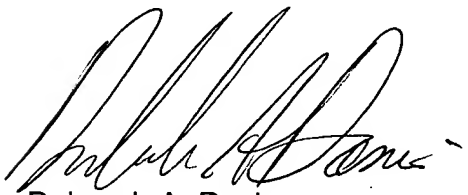
Conclusion

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah A. Davis whose telephone number is (571) 272-0818. The examiner can normally be reached on 8-5 Monday thru Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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March 5, 2005

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05/07/05